
International Task Force for Prevention Of Coronary Heart Disease



Coronary heart disease and stroke: Risk factors and global risk

Homocysteine, heart disease and stroke

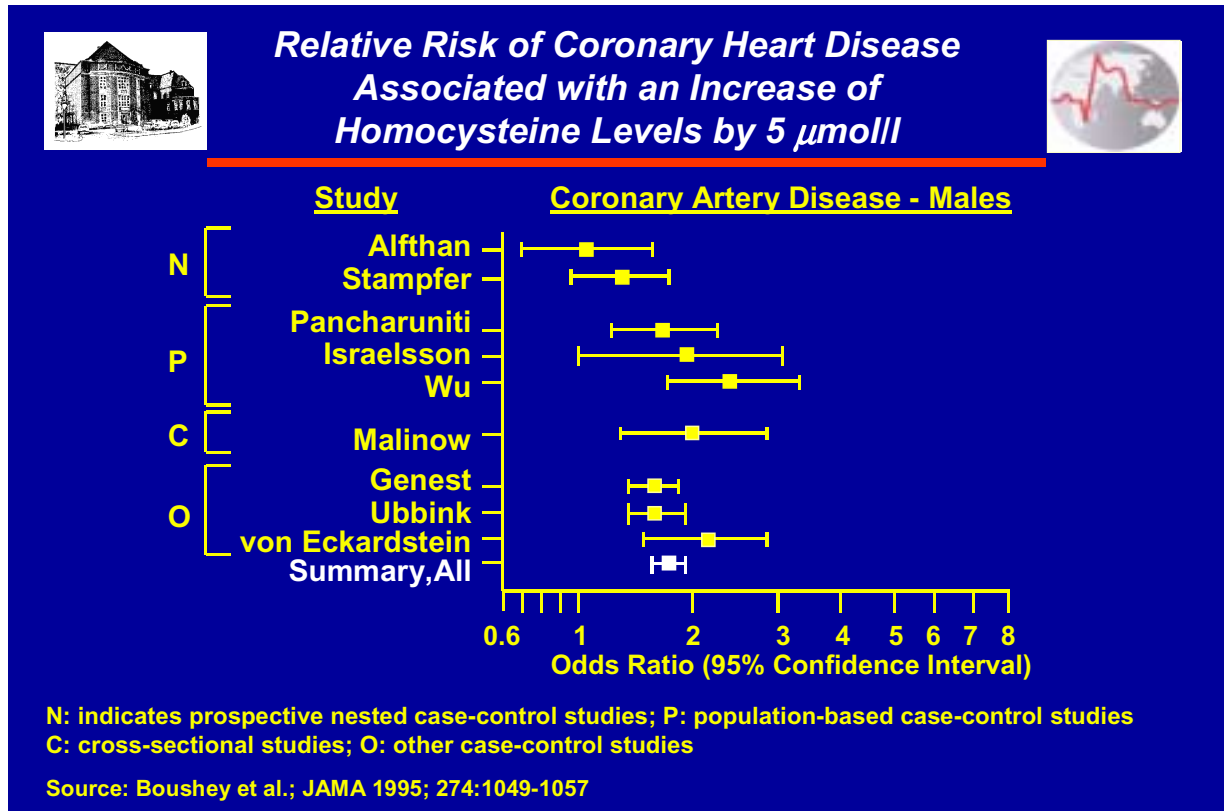
In recent years homocysteine has been identified as a potential risk factor for coronary heart disease and stroke.
This slide kit summarises major findings.

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Slide 1:

Risk of coronary heart disease associated with an increase of homocysteine

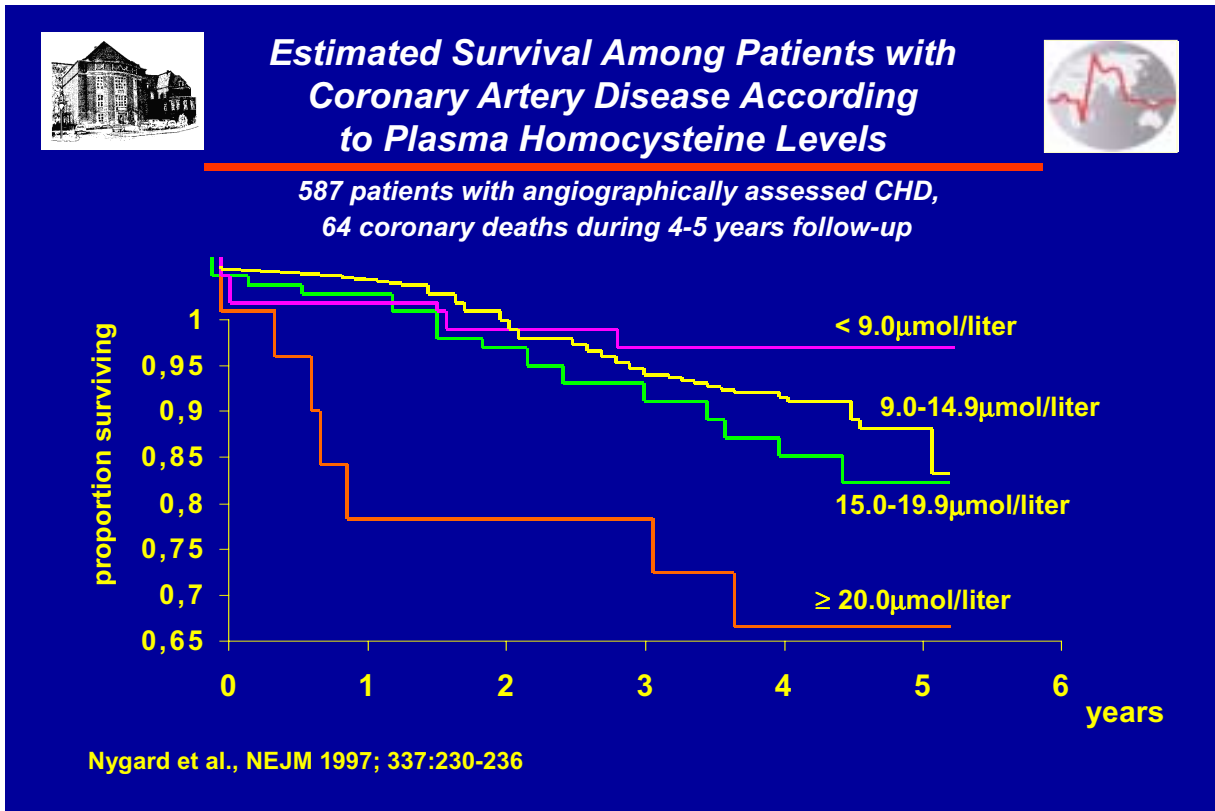


Risk of coronary heart disease associated with an increase of homocysteine

Various case-control studies demonstrate that homocysteine levels in plasma are higher in patients with coronary heart disease than in controls. In a meta-analysis of various studies, an increase of homocysteine by 5 $\mu\text{mol/l}$ was found to increase the risk for coronary heart disease by a factor of approximately two.

Slide 2:

Estimated survival among patients with coronary artery disease according to plasma homocysteine levels



Estimated survival among patients with coronary artery disease according to plasma homocysteine levels

In this follow-up study of individuals with angiographically assessed coronary heart disease patients with a homocysteine level below 9 μmol/l had a considerably better life expectancy than individuals with homocysteine levels above 20 μmol/l.

Slide 3:

The role of homocysteine as an independent cardiovascular risk factor



The Role of Homocysteine as an Independent Cardiovascular Risk Factor May be Limited by its Correlations with Age, Fibrinogen, D-dimer, and C-Reactive Protein



	lg_e homocysteine	number of coronary arteries >50% stenoses
age	0.343**	0.282**
lg_e fibrinogen	0.258***	0.198**
lg_e D-dimer	0.252***	0.303***
lg_e CRP	0.098*	0.084*
lg_e homocysteine		0.199**

* P < 0.05; ** P < 0.01; ***: P < 0.001.

(Univariate correlations between homocysteine, number of stenosed coronary arteries, and possible confounding factors in 348 men and 117 women.

Upon multivariate analysis, only the association of D-dimer with CHD was significant.
After exclusion of D-dimer, only the association with fibrinogen was significant)

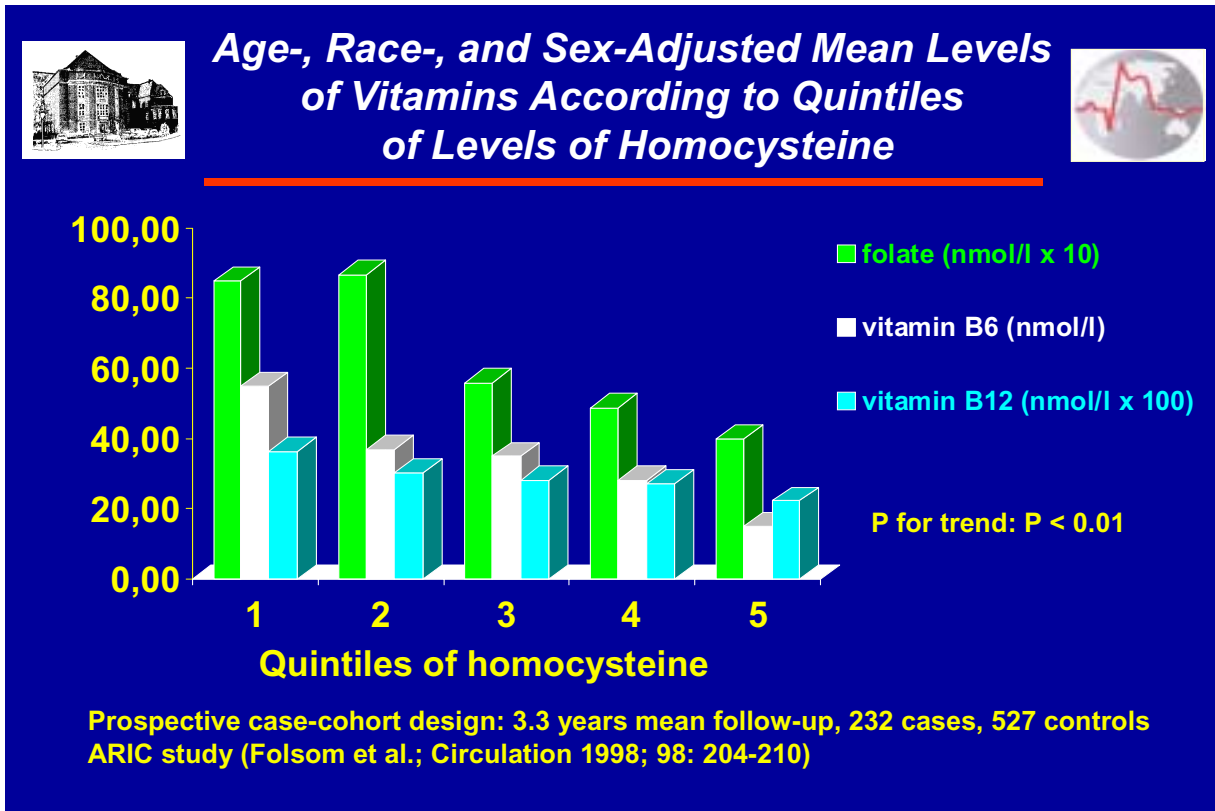
von Eckardstein et al.; ATVB 14: 460-464, 1994 von Eckardstein & Assmann; NEJM 337:1631, 1997

The role of homocysteine as an independent cardiovascular risk factor

It is here demonstrated that various risk factors for coronary artery disease correlate with both homocysteine plasma concentration and the number of stenosed coronary vessels. This highlights important inter-relationships between risk factors and coronary artery disease.

Slide 4:

Relationship between vitamins and homocysteine

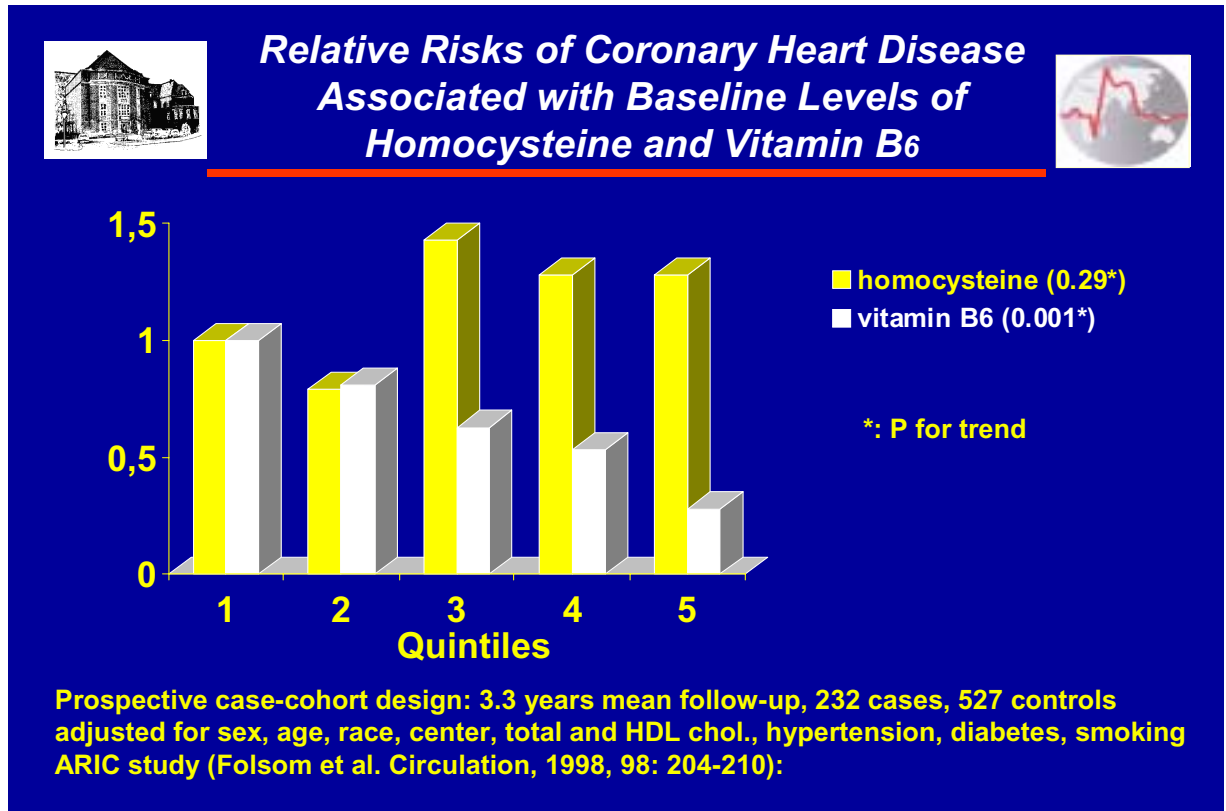


Relationship between vitamins and homocysteine

It is here demonstrated that serum levels of folate, vitamin B6 and vitamin B12 are correlated with the plasma concentration of homocysteine.

Slide 5:

Relative risks of coronary heart disease associated with baseline levels of homocysteine and vitamin B6

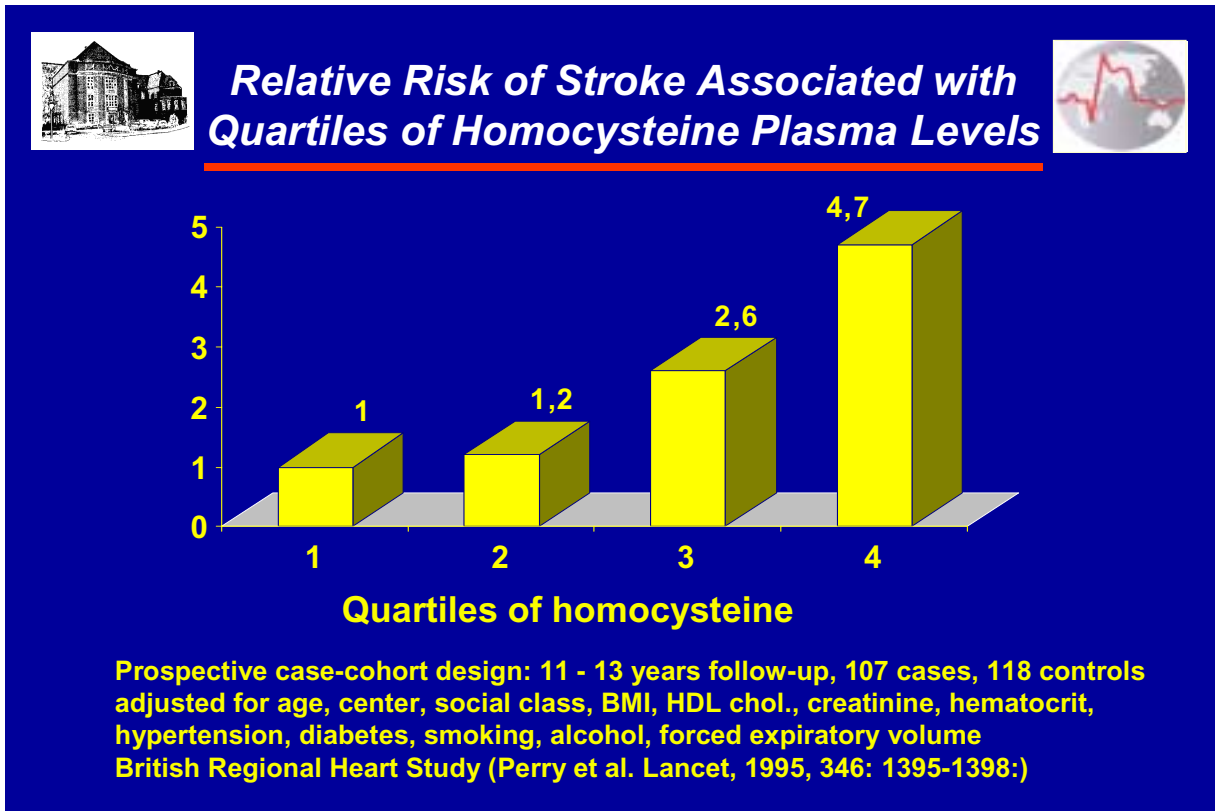


Relative risks of coronary heart disease associated with baseline levels of homocysteine and vitamin B6

This slide demonstrates that vitamin B6 exhibits an inverse association with the risk of myocardial infarction, while homocysteine had no significant association. Based upon these data it cannot be excluded that vitamin B6 is a more important risk factor than homocysteine and that high homocysteine levels reflect the cardiovascular risk exerted by vitamin B6 deficiency.

Slide 6:

Risk of stroke associated with homocysteine plasma levels

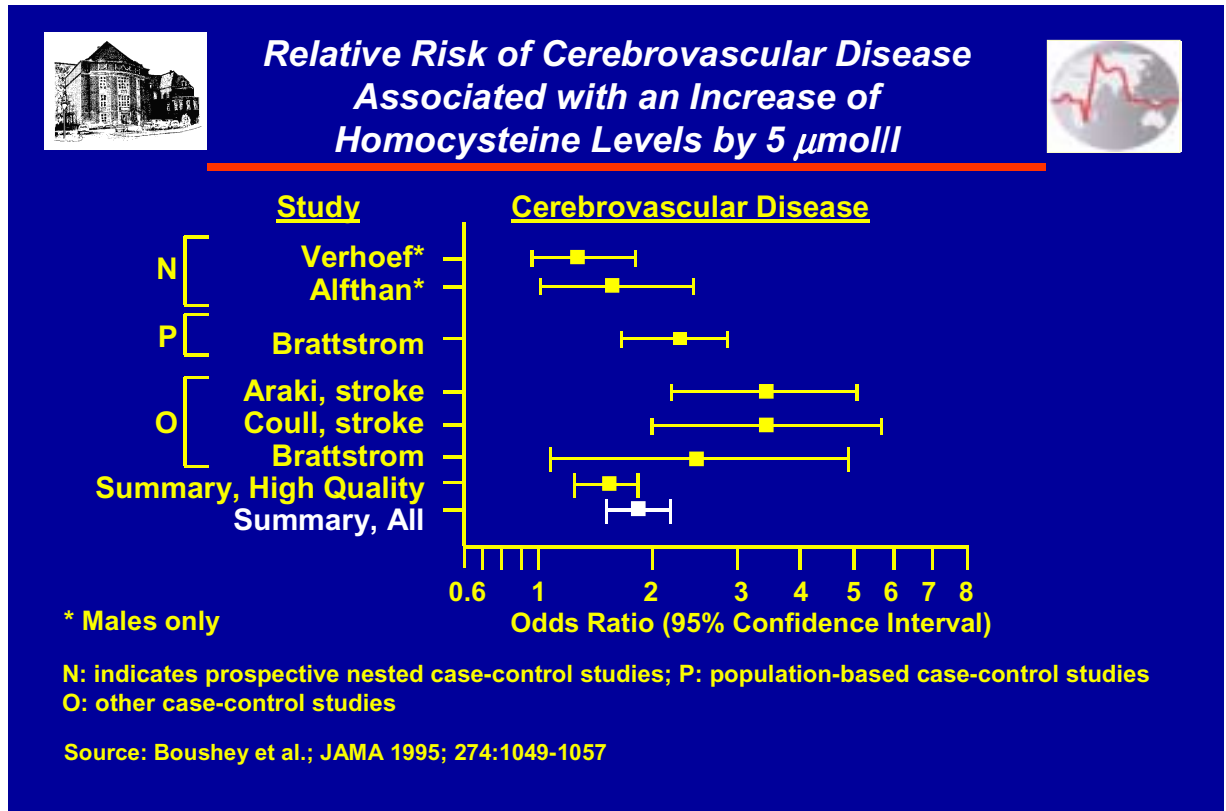


Risk of stroke associated with homocysteine plasma levels

It is here demonstrated that homocysteine may not only be a risk factor for coronary heart disease but also for stroke.

Slide 7:

Risk of coronary heart disease associated with an increase of homocysteine

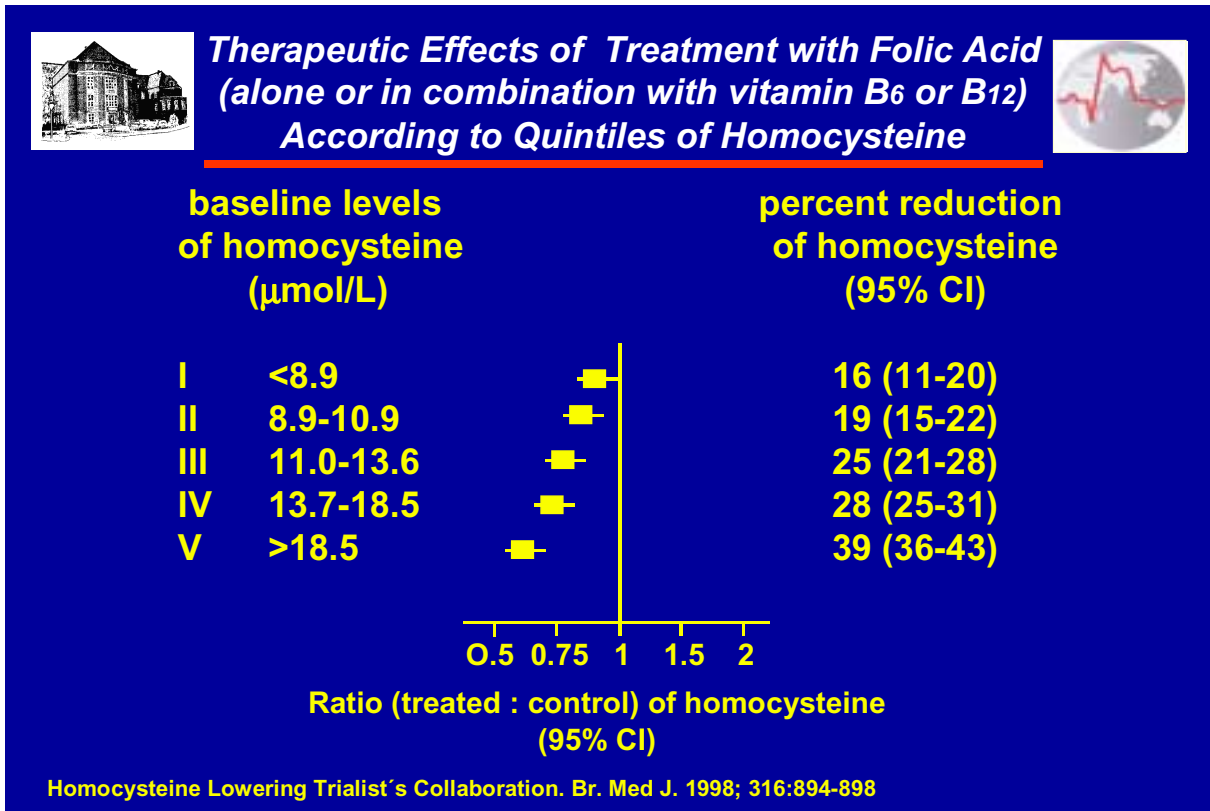


Risk of coronary heart disease associated with an increase of homocysteine

Similar to coronary heart disease, in various case-control studies an increase of homocysteine levels by 5 $\mu\text{mol/l}$ increases the risk of stroke by a factor of 1.5 to 2.

Slide 8:

Therapeutic effects of treatment with folic acid according to quintiles of homocysteine



Therapeutic effects of treatment with folic acid according to quintiles of homocysteine

A recent meta-analysis has revealed that vitamin treatment produces the greatest percentage reduction of homocysteine (39%) in individuals with the highest baseline levels of homocysteine, e.g. >18 µmol/l.

Slide 9:

Should hyperhomocysteinemia be treated ? (part 1)



Should Hyperhomocysteinemia Be Treated? (Part 1)



Arguments favouring treatment

- **Approximately 80 clinical and epidemiological studies suggest that elevated homocysteine is a risk factor for coronary heart , cerebrovascular, and peripheral vascular diseases**
- **Risk factor treatment of cardiovascular disease is an accepted clinical practice**
- **Treatment is inexpensive and unobtrusive under medical supervision**

Should hyperhomocysteinemia be treated ? (part 1)

There is currently a scientific debate about the need of treatment of hyperhomocysteinemia. Large trials are currently being conducted, aiming to resolve this issue. Arguments pro and contra treatment are listed on this and the following slide.

Slide 10:

Should hyperhomocysteinemia be treated ? (part 2)



Should Hyperhomocysteinemia Be Treated? (Part 2)



Arguments against treatment

- **Six prospective studies were predictive of vascular disease, but five were not**
- **No data from clinical intervention trials are available which demonstrate benefits towards prevention of cardiovascular endpoints**

Should hyperhomocysteinemia be treated ? (part 2)

There is currently a scientific debate about the need of treatment of hyperhomocysteinemia. Large trials are currently being conducted, aiming to resolve this issue. Arguments pro and contra treatment are listed on this and the previous slide.

Slide 11:

Homocysteine and cardiovascular disease: Recommendations of the International Task Force for the Prevention of Cardiovascular Disease



Homocysteine and Cardiovascular Disease: Recommendations of the International Task Force for the Prevention of Cardiovascular Disease



- 1. Homocysteine should be measured in patients with history of atherosclerotic and/or thromboembolic vessel diseases**
- 2. Individuals with homocysteine levels $> 12 \mu\text{mol/l}$ should increase and/or supplement the dietary intake of folic acid**
- 3. Patients with homocysteine levels $> 30 \mu\text{mol/l}$ should be treated with daily doses of 400-800mg folic acid, 2-4mg vitamin B₆ and 400mg vitamin B₁₂**

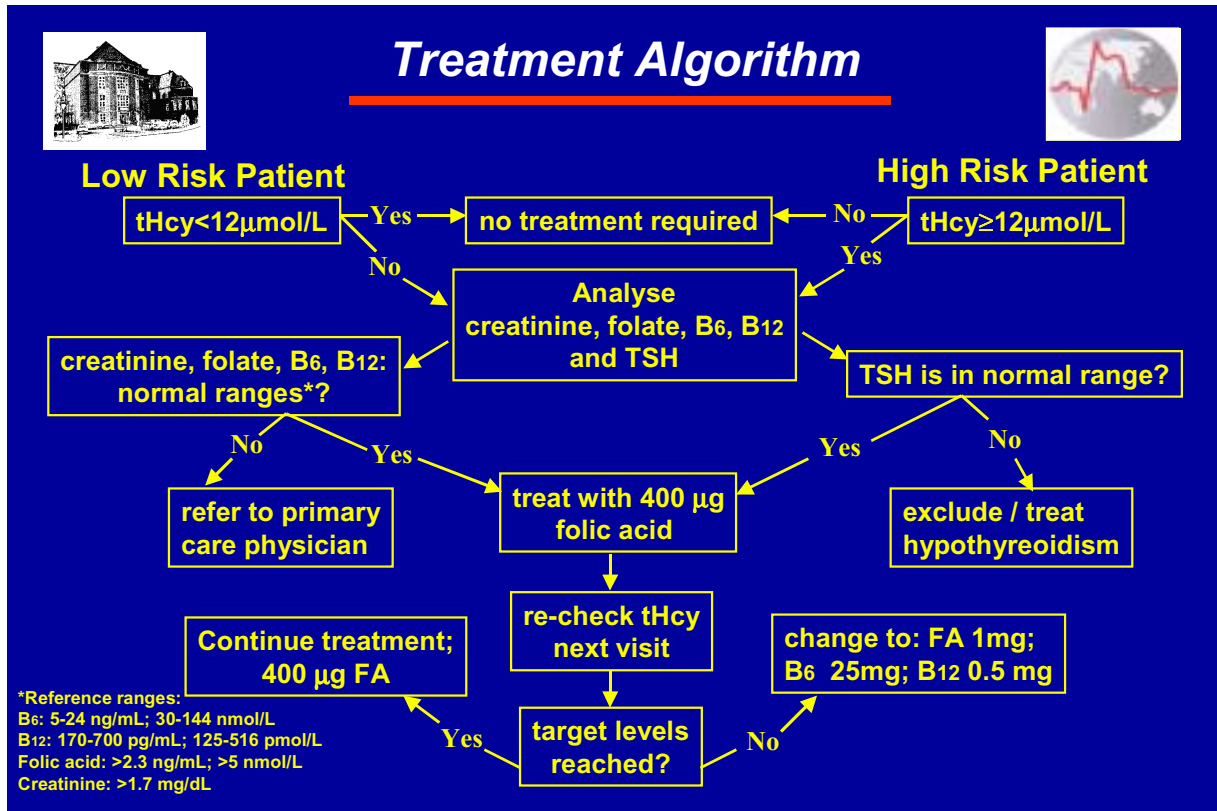
Nutrition, Metabolism, and Cardiovascular Disease 1998, 8:212-271

Homocysteine and cardiovascular disease: Recommendations of the International Task Force for the Prevention of Cardiovascular Disease

According to current practice, homocysteine levels $> 12 \mu\text{mol/l}$ deserve attention. In major sub-groups of individuals dietary intake of folic acid is sufficient to normalise homocysteine levels (see slide 13).

Slide 12:

Treatment algorithm



Treatment algorithm

This is a more detailed treatment algorithm for hyperhomocysteinemia. Note, that thyroid and kidney function as well as vitamin deficiencies should be ascertained.

Slide 13:

Food rich in Folic acid, Vitamin B6, and Vitamin B12



***Food Rich in Folic Acid,
Vitamin B6, and Vitamin B12***



Folic Acid

Vitamin B6

Vitamin B12

**vegetables
potatoes
full grain cereals
soya products
meat
eggs
milk products**

**pork and poultry
fish
cabbage
legumes
full grain cereals
soya products**

**meat
fish
eggs
milk products**

Food rich in Folic acid, Vitamin B6, and Vitamin B12

Mild elevation of homocysteine can be frequently corrected by dietary means.